component part and its operation to other parts and their operations. In the early 1960s de Duve and others succeeded in piecing together such an account of the lysosomal system (Bainton, 1981).

As shown in Figure 6.16, de Duve presented parallel versions of the mechanism for the digestion of material entering the cell from without (heterophagy) and from within (autophagy). In heterophagy, the material to be digested by the lysosomal enzymes was first entrapped into what he called a *phagosome*. He proposed these vesicles then fused with the lysosome sac, which he called the *primary lysosome*, creating a digestive vacuole or *secondary lysosome*. Some of the digestion products diffused back into the cytoplasm of the cell while materials resistant to attack built up in the vacuole, creating what he called a *residual body*, which either was expelled or continued to build up in the cell. In autophagy, de Duve called the digestive vacuole an *autophagic vacuole*; these were operated on in the same manner as phagosomes. He developed a technique for staining for the activity of acid phosphatase, using lead to generate an insoluble compound that has a high electron scattering potential. This yielded a dark image in the micrographs that enabled visualization not only of the lysosome itself but also of the digestive vacuole, autophagic vacuole, and residual body. Inside the autophagic vacuoles, it was possible to recognize remnants of mitochondria and the endoplasmic reticulum (de Duve, 1963).

A last piece of the story of the lysosome is an account of its formation in the cell. Because hydrolytic activity is the defining mark of the lysosome, the discovery of acid phosphatase also in some cisternae of the *trans* region of the Golgi apparatus and in adjacent smooth endoplasmic reticulum led Novikoff and his colleagues to designate the area GERL (a Golgi-related region of smooth endoplasmic reticulum from which lysosomes appear to develop) (Holtzman, Novikoff, & Villaverdi, 1967). Novikoff advanced the idea that hydrolases bypass the Golgi stack and are transported directly to the most distal area of the Golgi apparatus for incorporation into primary lysosomes.

Research on the lysosome by de Duve encapsulates the productive coordination of the results of structural and functional decomposition in discovering cell mechanisms. Modifying the techniques of cell fractionation, he identified a new fraction whose contents indicated their function. Moreover, their operation turned out to require isolation if they were not to destroy the cell itself. Comparing electron micrographs of the fraction with micrographs of cells revealed the locus of the organelle in the cell. At this stage the lysosome had a structural identity and a function, but understanding its operation required postulating other components, whose existence could also be identified in